Appendix A

Version of Replacement Sections For the Specification with Markings to Show Changes Made

Replace the title on page 1, line 1, with the following new title;

--<u>Rigid Reticulated Articles and </u>[Process] <u>Processes</u> for Producing Rigid Reticulated Articles--.

Replace the paragraph beginning on page 2, line 12 and ending on page 2, line 20 with the following paragraph:

--By and large, metal or ceramic materials that have been proposed for bone substitutes have been of low porosity. The art contains examples of substantially dense metals and ceramics with a semi-porous surface which is filled or coated with a calcium phosphate based material. The resulting structure has a dense metal or ceramic core and a surface which is a composite of the core material and a calcium phosphate, or a surface which is essentially a calcium phosphate. The bone substitute materials of this type commonly are heavy and dense, and often are significantly stiffer in structure than bone. Reference here is made to U.S. Patents 5,306,673 (Hermansson et al.), 4,599,085 (Riess et al.), 4,626,392 (Kondo et al.), and [4,967,509] <u>4,957,509</u> (Tamari et al.).--.

Replace the paragraph beginning on page 2, line 21 and ending on page 3, line 2 with the following paragraph:

--In addition to bone substitute materials described above, there are other applications in which the chemical, thermal, or other properties of a ceramic, metal, or other material can best be used in a porous form. One form of rigid porous materials with

utility is the reticulated foam. A foam material is one with a large degree of volumetric porosity. This porosity is ideally fully open and fully interconnected. A common method of manufacture of these types of materials is to coat the surfaces of a polymeric foam with a slip of ceramic or metal, and then burn out the foam and other organic. The ceramic or metal coating is then sintered to leave a rigid foam with a structure largely similar to the starting polymeric foam. There are numerous examples of cellular, rigid foams in the known art and processes for producing these materials. See, for example, U.S. Patent Nos. 4,000,525 and 5,061,660. However, the known art for producing [foam] rigid foam materials suffers from occluded openings and thus is not able to achieve a substantially fully open and interconnected porosity.--.

Replace the section beginning on page 4, line 11 and ending on page 4, line 13 with the following section:

--(e) optionally contacting the reticulated substrate with one or more additional [dispersion] <u>dispersions</u> to form one or more additional coatings wherein the one or more additional coatings are the same or different from each other and the first coating;--.

Replace the paragraph beginning on page 6, line 17 and ending on page 6, line 22 with the following paragraph:

--In yet another embodiment, the process provides struts which are comprised of a mixture or composite which contains the supportive material as well as osteoconductive material, the [support] <u>supportive</u> material providing strength to the article and the osteoconductive material being carried at least partially on the surface of the interstices so as to be exposed to the interconnected openings to provide an osteoconductive

environment favoring bone growth.--.

Replace the paragraph beginning on page 8, line 26 and ending on page 9, line 16 with the following paragraph:

--The continuous [supporting] <u>supportive</u> framework having interconnecting interstices or openings may be considered to be the primary load bearing element, and the osteoconductive material commonly is much weaker than the supporting framework. The [supporting] <u>supportive</u> framework is preferably formed, as mentioned above, of a ceramic material such as zirconia. The framework structure is formed such that the interstices or openings themselves, on average, are wider than are the thicknesses of the struts which separate neighboring interstices. The load bearing framework is essentially completely continuous and self interconnected in three dimensions, and the void portion is also essentially completely continuous and self interconnected in three dimensions. These two three dimensionally interconnected parts are intercolated with one another. This can be referred to as a 3-3 connectivity structure where the first number refers to the number of dimensions in which the load bearing framework is connected, and the second number refers to the number of dimensions in which the void portion is connected. The concept of connectivity is explained at greater length in Newnham et al. "Connectivity and Piezoelectric-Pyroelectric Composites," Materials Research Bulletin, Vol. 13 pp. 525-536 (1978), the teachings of which are incorporated herein by reference. With the supporting framework described herein, the framework itself is given a 3 as it is connected in 3 dimensions, and the void portion is treated likewise. In contrast, partially sintered assemblages of powders invariably contain isolated pores or voids which are not

connected to all other voids. A material with all isolated (that is, dead end) pores in a dense matrix would have 3-0 connectivity. A material having pores that pass completely through the matrix in one dimension would yield 3-1 connectivity, and a material having pores that interconnect two perpendicular faces but not the third would have 3-2 connectivity.--.

Replace the paragraph beginning on page 9, line 17 and ending on page 10, line 3 with the following paragraph:

--The opening sizes in the supportive framework preferably are at least about 50 μm and preferably are on the order of 200 μm to about 600 μm. It is preferred that there be substantially no pores or voids less than 50 μm. It should be understood that the openings in the supportive framework are of myriad irregular shapes. The interconnected openings or interstices through which biological ingrowth processes can take place define in three dimensions a labyrinth in which bone ingrowth and vascularization can occur; that is, the openings have many junctures with other openings to thus define tortuous pathways through the framework. In general, it is believed that in order to adequately support the growth of bone into the framework openings, the openings must be capable of accommodating the passage of tissue having transverse dimensions of at least about 50 μm. Conceptually, it is convenient to think of a 50 μm opening in materials of the invention as being capable of accommodating the passage through it of a "worm" having a round cross section and a transverse diameter of 50 μm. Put another way, a 50 μm opening should enable passage through it of a sphere having a 50 μm diameter. Although there is no completely satisfactory way known to us for measuring the opening sizes, it is

possible to examine a scanning electron micrograph of a cross section of an article of the invention and viewing it as a planar projection of the structure, drawing several lines across the micrograph, measuring the openings that are intersected by the lines, and using averaging and standard deviation techniques to permit the size of the openings to be assessed.--.

Replace the paragraph beginning on page 10, line 8 and ending on page 10, line 18 with the following paragraph:

--Zirconia and other ceramics, when used to form the supportive framework, are exceedingly hard and are far more rigid than is bone. Although it would be desirable to employ as the supportive framework a material having a modulus of elasticity nearer to that of bone, bone substitute materials of the invention employing rigid materials having quite open interstices work well. It is believed that the ultimate union of bone with such porous articles during the healing process occurs over a large surface area and depth as the encroaching bone penetrates deeply into the interstices of the article. The substantial bone/ceramic interface that results enables forces to be readily transmitted to and from the ceramic framework with significantly less stress concentration in comparison to [structure] structures resulting from a bone/ceramic union that occurs within a small area of surface-to-surface contact and with little or no penetration of bone into the article.--.

Replace the paragraph beginning on page 14, line 2 and ending on page 14, line 11 with the following paragraph:

--Pieces of the zirconia prepared as described above[-]were immersed in the slip and mechanically agitated to remove air bubbles and to assure complete penetration of the

slip into the openings. Excess slip was allowed to drain, and further slip was removed with a stream of compressed air. The pieces were dried and were then raised at the rate of 5°C per minute to a sintering temperature of 1400°C and were held at this temperature for one hour. The resulting product comprises a strong ceramic framework of zirconia, the struts of which have a surface layer comprised of 75 volume percent zirconia and 25 volume percent hydroxyapatite. The structure of this product is illustrated in Figure 1, and note may be made of the open nature of the [supporting] zirconia [supporting] <u>supportive</u> framework and the 3-3 connectivity of the framework and the hydroxyapatite.--.

Replace the paragraph beginning on page 15, line 5 and ending on page 15, line 8 with the following paragraph:

--Depending upon the relative amounts of zirconia and hydroxyapatite that are used, the hydroxyapatite may appear as small "islands" on the surface of the struts; this is illustrated in Figure 3. Sufficient hydroxyapatite or other osteoconductive material is employed so <u>as to</u> provide the surface of the struts with osteoconductive properties.--.

Replace the paragraph beginning on page 15, line 18 and ending on page 15, line 26 with the following paragraph:

--A dispersion is made by combining a metal powder or a ceramic powder with a binder[,] and a solvent which is then contacted with a reticulated substrate to coat the substrate with the dispersion. The term "dispersion" is used synonymously with the term "slip" described above, in that both terms refer to a solvent which suspends a ceramic or metal powder, a binder and optional additives. After contacting the substrate with the dispersion, the substrate is removed and may be drained to allow removal of excess

dispersion. Additional excess dispersion may be removed by rollers or by a jet of compressed air as described above. The coated substrate is then dried to remove at least a portion of the solvent. Drying may be accomplished by ways well known in the art.--.

Replace the paragraph beginning on page 15, line 27 and ending on page 16, line 8 with the following paragraph:

--In a preferred embodiment, the binder becomes solvent-insoluble and flexible upon drying. Preferably, the binder is employed as a relatively large volume fraction of the dispersion. The volume fraction can be at least 25 vol. %, more preferably at least 50 vol. % based on the entire volume of the solid components of the dispersion following drying. The use of such a binder, particularly at a relatively large volume fraction, provides an insoluble flexible film on the substrate that can be subsequently deformed without substantially cracking off, flaking off, or peeling off of the substrate. As used herein, "without substantially cracking off, flaking off, ..." means that upon deformation, less than 10wt %, preferably less than 5 wt %, based on the dried weight of the coating, and more preferably none of the coating is removed from the substrate. A preferred binder is a polyacrylate emulsion that polymerizes upon drying. While curing (i.e., polymerizing) by drying is preferred, any other means of curing such as the use of catalysts, radiation or gellation [to initiate] are also contemplated. Other preferred binders can include any polymer which [become] <u>becomes</u> substantially insoluble in the carrier solvent upon drying.--.

Replace the paragraph beginning on page 18, line 9 and ending on page 18, line 19 with the following paragraph:

--As noted above, one advantage of the present invention is that smaller porosity substrates may be used and the resulting reticulated article will still have the open interconnected porosity. The substrates may have at least 20, 50, 80, or 100 pores per inch or even greater, depending on the particular application. Suitable substrates can include polymeric foams, such as the polyester, polyurethane, polyether, and polyester-polyurethane foams described above and even natural sponges. Preferably, the substrate is "compliant" which is defined as deforming upon the application of an external force. The deformed substrate returns to at least a portion of, and preferably substantially all of its pre-deformation shape after the external force is removed. The substrate is preferably also wettable. Wettable in this instance is defined as being wettable [with] by the solvent alone, or being rendered wettable by the use of known wetting agents.--.

Replace the paragraph beginning on page 20, line 15 and ending on page 20, line 19 with the following paragraph:

--A reticulated structure with struts having a core of partially stabilized zirconia, an intermediate layer of zirconia 25 volume % hydroxyapatite composite (ZHA-25), and a surface layer of hydroxyapatite calcium phosphate ceramic was prepared. First, ceramic dispersions were prepared of zirconia, ZHA-25, and hydroxyapatite [were prepared] as follows.--.

Replace the paragraph beginning on page 22, line 3 and ending on page 22, line 7 with the following paragraph:

--A reticulated structure was prepared where the struts had a core of partially stabilized zirconia, an intermediate layer of zirconia 40 volume % - hydroxyapatite

composite, and a surface layer of hydroxyapatite calcium phosphate ceramic. First, ceramic dispersions were prepared of zirconia, zirconia-hydroxyapatite composite with 40 volume percent HA (ZHA-40), and hydroxyapatite [were prepared] as follows.--.

Replace the Abstract on page 32 with the following Abstract:

--ABSTRACT OF THE DISCLOSURE

A process for producing [for producing] a rigid reticulated article[, includes; (a) providing a first dispersion of a ceramic or metal powder, a binder, and a solvent; (b) providing] <u>involves coating</u> a reticulated substrate which has open, interconnected porosity[; (c) contacting the reticulated substrate] with [the] <u>a</u> first dispersion [to coat the substrate with the dispersion] <u>of a ceramic or metal powder</u> to form a first coating <u>thereon</u>; [(d)] drying the coated reticulated substrate; [(e)] contacting the <u>coated</u> reticulated substrate with one or more additional dispersions <u>in succession</u> to form one or more additional coatings [wherein the composition of the one or more additional coatings are the same or different from each other and the first coating; (f)] <u>thereon;</u> drying the additional [coating] <u>coatings</u> between the steps of contacting; [(g)] heating the coated reticulated substrate [at a time and temperature sufficient] to pyrolyze [any] organic components; and [(h)] sintering <u>the coated reticulated substrate</u> to form a [ceramic or metal or composite] reticulated article<u>, wherein each dispersion has a viscosity less than that of all preceding dispersions</u>. [In another aspect, the binder becomes solvent-insoluble and flexible upon drying. According to this aspect, one or more additional coatings may optionally be used. In another aspect, a method for forming a ceramic article useful as a bone substitute and having an outer surface defining a shape having a bulk volume and having open, interconnecting openings extending throughout the volume and opening through the

surface, includes, providing an organic open-pore structure, coating surfaces of pores of the structure with a ceramic slip, pyrolyzing the organic structure to leave a ceramic structure having struts defining a plurality of interconnecting interstices, and providing within the interstices an porous osteoconductive composition exposed to the interconnecting openings. In a preferred embodiment, the ceramic slip includes a strong, supportive ceramic material and a separate osteoconductive material. In another aspect, a] A rigid reticulated article includes[, a first sintered ceramic or metal or composite material having an outer surface defining a shape having a bulk volume, interconnecting openings extending throughout the volume and opening through the surface, and struts bounding the interconnecting openings, wherein the material has at least 20 openings per inch] inner, intermediate and outer sintered layers of material in which the inner and outer layers are of different composition and the intermediate layer is a composite of the inner and outer layers.--.